Decision-making in severe traumatic brain injury: patient outcome, hospital costs, and research practice

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CHAPTER 12

GENERAL DISCUSSION AND FUTURE PERSPECTIVES

Humans have suffered from the consequences of traumatic brain injuries (TBI) from the beginning of mankind and will continue to do so in the future. For ages, people have attempted to minimize the consequences of TBI by examining and treating affected individuals. [1] Extensive experience and improvements in medical treatments from the last century resulted in substantial progress in the survival and outcome of severe TBI (s-TBI) patients (Glasgow Coma Score (GCS) of 3 – 8). [2-5]

Patients with s-TBI (29% – 40%) [6,7] and vs-TBI (GCS 3 – 5; 19.6% – 23%) [6,7] are nowadays able to achieve so-called 'favourable' outcome. [8,9] Most s-TBI patients (40% – 65%) [6,7] however still die or survive with long-term disabilities [2,3,8-11], which also negatively affects the quality of life of most proxies. [12-14] Outcome is usually worse in patients with higher TBI severity (i.e. lower GCS, pupillary abnormalities), intracranial abnormalities on first CT scan, extracranial injuries and need for surgical intervention. [3,6,7,15-17] Despite all available patient outcome data, it remains challenging to interpret, generalize, valuate, and use this data for acute treatment decision-making.

Acute treatment decisions are poorly supported by high- or even moderate quality evidence and accurate prognostic algorithms, leaving ample room for uncertainty.[18-23,47] Also, available guidelines do not cover all relevant topics due to a lack of supporting evidence. [18] Non-adherence to guidelines and treatment variation seem understandable in light of such lack of certainty. [24-27] It even remains unclear how specific factors substantiate the acute treatment decision-making process. [28-31] As a result, the decision to initiate acute treatment or not in s-TBI patients or discontinue critical care in the subacute period poses major medical and ethical dilemmas to physicians.

This *general discussion* elaborates on the role of patient outcome and in-hospital costs in the acute treatment decision-making process in s-TBI patients.

Main findings and interpretation

Patient outcome

Providing healthcare is about doing 'right' for individual patients and about better health for populations. [32] Physicians have a responsibility to customize treatment strategies to achieve best possible patient outcome that is respectful of and responsive

to individual patient preferences, needs, and values. [32] Choosing an acute treatment strategy that is proportional and leads to best possible patient outcome is however difficult. This is mainly caused by uncertainties on future patient outcome, especially regarding outcome prediction and outcome valuation.

Patient outcome prediction

Because providing healthcare is about patient outcome in the future, it is necessary to use a prediction of that outcome for acute treatment decisions. Knowing what specific outcome will be achieved after a specific treatment is likely to improve decision-making. [30,31,33-35]

Unfortunately, physicians appear to be unable to make accurate outcome predictions (Table 1). [22,33,36,37] Validated prognostic models, such as IMPACT and CRASH [38,39], have been developed to assist physicians with TBI outcome prediction, but they have not been widely implemented in clinical care. [40-44] Although IMPACT and CRASH models display good discriminative ability in validation studies [40,41], they are, like experienced physicians, considered to be too inaccurate on individual level predictions. Heterogeneity between individual patients with variable injuries, pathophysiology, and treatments makes prognostication difficult and uncertain. Another limitation of available prognostic models is that they only include robust short-term outcome measures like mortality and functional outcome. Although robustness is a good epidemiological attribute of clinical studies it misses personal human properties like long-term physical, cognitive, emotional and behavioural outcome, or satisfaction with life. [33,38-45] This is problematic, because these long-term consequences of s-TBI are highly relevant to include in outcome assessment. [46]

Table 1. Difficulties in outcome prediction in TBI patients (chapter 6) [47]

#	Difficulties in random order.
1	The heterogeneous nature of s-TBI and concurring comorbidities and their unknown effect on outcome.
2	Unclear/incomplete clinical information, including the patient's neurological state and level of consciousness.
3	Largely unknown pathophysiological mechanisms of brain injury and inherent degree of brain plasticity.
4	Prediction models do not include long-term (health-related) quality of life, although long-term changes have been reported and patients/proxies are known to value this outcome.
5	Prediction models are based on large retrospective data sets that do not necessarily reflect current or future treatment strategies.

High prognostic accuracy is indispensable when a prediction is used to substantiate individual acute treatment decisions. Relatively small mathemathical inaccuracies

can have disastrous clinical consequences. It remains unknown how high this accuracy must be and what cut-offs should be used for decision-making. There are peer reviewed recommendations that consider it reasonable to pursue non-aggressive care in patients with a >85% chance of death or 'unfavourable' outcome. [34] If a physician would have followed this recommendation, a 28-year old patient with a CRASH-model predicted risk of death at 14 days of 91.8% and a risk of an 'unfavourable outcome' at 6 months of 95.7%, that achieved 'favourable' outcome and was able to live independently, would have probably died after treatment-limiting decisions. [48]

Despite many efforts to improve outcome prediction, there is substantial inaccuracy in todays' prognostic abilities. Every effort must be made to prevent that patients are unfairly deprived of potentially beneficial care because of erroneous prognostication or poorly chosen cut-offs. It is therefore essential that inherent uncertainties of outcome prediction are acknowledged in the acute decision-making process. Only the best possible approximation of expected patient outcome should be used and opportunities to improve prognostic accuracy should be explored.

Patient outcome valuation

Valuation of predicted patient outcome is about judging the favourability of a patients' future health status and about defining how 'acceptable' or 'unacceptable' that health status is to patients, proxies and societies. Its importance for acute treatment decision-making seems obvious. Common sense dictates that acute treatment should be initiated or continued when outcome is judged 'acceptable', and withheld or discontinued when outcome is judged 'unacceptable'.

A cut-off point for 'acceptability' of outcome would be useful, but an exact definition of 'acceptable' or 'unacceptable' outcome remains elusive, and is probably impossible to determine. [49,50] Any cut-off point will be highly arbitrary and can never account for the countless outcome possibilities and numerous variations in peoples' specific contexts, and ever-changing desires or interpretations of well-being or 'the good life'. Life can be judged worth sustaining because it has intrinsic value to relatives and friends, or because of cultural or religious reasons. [51] *(chapter 6)*

Several scales and checklists have been developed to quantify the individual and societal impact of TBI, and to improve the assessment of medical treatment efficacy. [52] Nonetheless, the most frequently used measures have important limitations in specifying the individual 'acceptability' of outcome. The reliability of

these measures for outcome valuation and their usefulness in the acute decision-making process of s-TBI patients remains disputed.

Patient mortality

The most frequently used and most straightforward outcome measure. Death is usually considered to be the worst possible outcome that should be prevented at any cost. [53] However, in s-TBI patients, survival with severe post-traumatic deficits can be a fate worse than death. [54-58] When considering the possibility of very severe cognitive, emotional, and physical disabilities, life and death are not necessarily equal to 'acceptable' and 'unacceptable'. As such, acute treatment decisions should not solely be based on predicted mortality.

Functional outcome

The Glasgow Outcome Scale (GOS) is the most highly cited outcome measure in brain injury studies. [59-61] Its use as TBI outcome measure is recommended by many organizations. [60] It assesses multiple aspects of life to determine the impact of TBI on patient functional outcome with a focus on social recovery. It uses dichotomous endpoints, in which 'favourable' outcome (the ability to function independently, see Table 2), is usually considered to be the 'acceptable' outcome. The introduction of the Glasgow Outcome Scale Extended (GOSE) and the structured interview [61] have solved points of criticism on validity and lack of sensitivity in the higher functional end of the scale, but there are remaining issues. [52,60,61]

The 'favourable'/'unfavourable' division remains arbitrary and ignores a patients' or proxy's perception of satisfaction with life. Patients with severe disability who are dependent in daily life (defined as 'unfavourable') can still judge their health status to be 'acceptable'. [60] But the other way around is also possible. Some studies classify 'upper severe disability' (GOS-E) to be 'favourable', while probably most physicians, researchers and healthy individuals would classify this outcome as 'unacceptable' within their own social and cultural context. [50,62]

Instead of using dichotomized outcome, sliding dichotomy or proportional odds methods are considered to be more informative. These methods are increasingly popular, but still have insufficient sensitivity to detect all changes. Subtle changes can be highly valuable for a patients' wellbeing, without having a measurable impact on pre-defined categories. [60]

The GOS/GOSE is a very usefull functional outcome measure, but does not include the essential subtleties of well-being. The use of 'favourable' and 'unfavourable' as substitutes for 'acceptable' and 'unacceptable' outcome is inadequate. These terms should not be interpreted or used as such in acute treatment decision-making.

Table 2 Explanation of Glasgow Outcome Scale (- Extended). [61]

Glasgow Outcome Scale (GOS)	Glasgow Outcome Scale – Extended (GOSE)	Brief description	
2. Death	2. Death	Death	Unfavourable
3. Vegetative state	3. Vegetative state	Absence of awareness of self and environment	
4. Severe disability	6. Lower severe disability	Needs full assistance in daily life	
	7. Upper severe disability	Needs partial assistance in daily life	
9. Moderate disability	10. Lower moderate disability	Independent, but cannot resume work/ school or all previous social activities	Favourable
	11. Upper moderate disability	Some disability exists, but can partly resume work or previous activities	
8. Good recovery	12. Lower good recovery	Minor physical or mental deficit that affects daily life	
	13. Upper good recovery	Full recovery or minor symptoms that do not affect daily life	

Health-Related Quality of Life (HRQoL)

HRQoL measures focus on a patient's view on the impact of TBI and a certain health status on their (quality of) life. They are a multi-dimensional concept including physical, mental, emotional, and social functioning. Generic HRQoL instruments are designed to investigate particular interventions or populations. [63] Disease-specific HRQoL measures have been specifically designed for a disease and are assumed to be more sensitive to that disease, allowing more precise outcome information.

The Quality of Life after Brain Injury (QOLIBRI) is an example of a TBI-specific HRQoL measure. [64] The applicability of the QOLIBRI in s-TBI patients however remains unclear. Most s-TBI patients suffer from cognitive impairment and communicative difficulties. Patients are hardly able to complete the questions, and, likely for this reasons, the QOLIBRI has only been validated in patients without substantial post-traumatic cognitive restraints. [65] Proxies are often unable to adequately substitute a patients view. [52] The QOLIBRI cut-off point of 60 (score 0 to 100) for quantifying a 'good' HRQoL also remains unclear and is prone for subjectivity. [66] Generic HRQoL instruments like the SF-36, EQ-5D, or WHOQOL-BREF are also considered to be less useful in patients with moderate or severe TBI (GCS 3-12). [67,68]

Individualized approach

The alternative of simply asking individual s-TBI patients in the acute setting to value their predicted outcome could be helpful, but is impossible. Patients after s-TBI have an inability to participate in the decision-making process by definition and their preferences, needs, and values are therefore unknown. [31] Written advanced directives are rarely available and patients have rarely discussed preferences with proxies. [49,51] In addition, proxies, as surrogate decision-makers, are mostly unavailable, unprepared, confused by uncertainty and hope, and unequipped to fully understand the uncertainties of acute clinical decision-making. Proxies might even misjudge or misrepresent patients' preferences. [69,70]

As mentioned in *chapter 6*, even without mental incapacity due to s-TBI, individuals are generally unable to predict accurately what future quality of life would be 'acceptable' or 'unacceptable' to them. People often underestimate their ability to adapt to a level of disability they previously considered 'unacceptable'. [33] Survivors of s-TBI that had achieved a so-called 'unfavourable outcome' defined by the Glasgow Outcome Scale (Table 2) after a decompressive craniectomy, or their caregivers, appeared to have changed their perception of 'a good quality of life'. They were satisfied and would even have provided retrospective consent for the intervention. [71,72] This absence of a linear connection between disabilities and experienced quality of life is known as the disability paradox [73] and is also seen in patients suffering from locked-in syndrome or Duchenne. [72,74-76]

A physician's perspective

Given the reservations regarding a patient's or proxies preferences, it is inevitable that a physician's outcome valuation is included in the acute treatment decision-making process. Although physicians have an important role in protecting a patient's interests, their valuation and subsequent acute treatment-decisions might not always honour a patients' preferences. Their valuations can be influenced by local policy, specialized medical training, personal and professional experiences, but also by individual values, religious beliefs, and cultural background. This might jeopardize the objective selection of an individualized healthcare strategy that aims to achieve 'acceptable' patient outcome.

An important risk in decision-making is a physicians' strong belief in high mortality and 'unfavourable' outcome rates, as it is likely to contribute to clinical nihilism and the overall belief that treatment is ineffective. [47] This focus on poor prognosis is not necessarily in line with reported patient outcome [6,7] but might lead to withholding, withdrawing, or decreasing intensity of potentially beneficial treatment(s). The

negative feedback makes other involved carers (i.e. nurses) pessimistic, which can result in limited care efforts, which in turn negatively influences patient outcome. [77]

Not realizing their own contribution, worse outcome will initially confirm their individual beliefs and later spread by the inclusion in clinical studies or when included in prognostic models. [77] As much as 63% of deaths in trials investigating s-TBI patients were registered after decisions to withdraw life-sustaining therapies. [78] Trial mortality rates could have been influenced by this large number of withdrawals, and could further contribute to maintain the belief in poor prognosis, resulting in more withdrawals of care and worse outcome. [78] Physicians need to be aware of this self-fulfilling prophecy and its potential effect on treatment decision-making. [79]

Some restraint in treatment-limiting decisions in the acute phase might be prudent given the uncertainties on patient outcome prediction and outcome valuation and the irreversible consequences of these decisions.

Can we fix the acute treatment decision-making process?

Acute treatment decision-making in s-TBI patients is highly complex and many problems with uncertainty in outcome prediction and outcome valuation will be difficult to solve. Despite this complexity, physicians will continue to make treatment decisions at the best of their abilities. An improvement in the quality of these inevitable acute treatment decisions could be achieved by deliberately delaying early treatment-limiting decisions in s-TBI patients with substantial prognostic uncertainty. This may not only prevent premature treatment-limiting decisions, but also means that these patients will receive optimal acute treatment, which hopefully allows best possible recovery, probably at the cost of increasing neuro-critical care costs.

The necessity for more time

The proposed strategy provides more time to measure and collect early key critical care variables to improve prognostic ability and to reconstruct a patients' preferences, values, and treatment whishes. [31,80-82] This valuable information on clinical progress, neurological recovery, and a complete, objective and consistent evaluation of rapidly evolving imaging modalities (i.e. CT and MRI) only becomes available with extra time and will substantially improve diagnostics and prognostication. [83-86] More time also allows multidisciplinary counsel including moral deliberation on individual patient or proxy preferences. All this additional information is highly valuable, and indispensable for a decision-making process. [31,87,88]

Although delaying treatment-limiting decisions seems to be a viable solution to improve decision-making, it is not common practice. Treatment-limiting decisions are reported within 2 days after injury in up to 70% of s-TBI patients. [78,89,90] Although physicians have best intentions, these early decisions deprive patients of a chance for succesfull recovery and usually result in clinical deterioration and death. [78,89] Limiting treatment within 2 days after injury seems to be disproportional and morally unjustified given the uncertainties on future outcome. [82]

It remains unknown how much extra time is necessary to sufficiently improve prognostic accuracy to avoid the withholding of potentially beneficial treatments. The Neurocritical Care Society recommends to use a 72-hour observation period for devastating brain injury patients to determine clinical response and delay decisions regarding withdrawal of life-sustaining treatment. [91] Longer decision-making intervals of a week or even 10 days have also been recommended, awaiting adequate control of cerebral edema, injurious neuroinflammation, and associated intracranial hypertension. [92,93] Delaying any conclusions about prognosis to after 72 hours is also advised for brain injury after cardiac arrest. [94]

Treatment-limiting decisions

There are advantages of the proposed strategy, but an unrestricted endeavour for sustaining life by providing optimal acute treatment to all s-TBI patients is undesirable and unrealistic for two main reasons:

First, providing acute treatment might be considered disproportional from a patients perspective. Treatment can be against patients' and proxies' preferences and values. [78,89,95] When achieved outcome becomes 'unacceptable', or when a combination of different features indicates very low chances of regaining an 'acceptable' outcome, or when treatment has become disproportionate given the outcome, treatment-limiting decisions should be considered. Treatment-limiting decisions can be inevitable and morally justified. Death is unwanted, but catastrophic conditions such as unresponsive wakefulness syndrome or minimally conscious state are accompanied by very severe disabilities and enormous challenges for both patients and proxies that should not be disregarded. [96,97] Many will doubt this is a human life worth living. [98] *(chapter 6)*

Several reasons to consider early treatment-limiting decisions are listed in textbox 1 *(chapter 6)*. [47] This list is meant to serve as a starting point for further discussion, rather than constitute a final list of reasons. Although all focus group participants from *chapter*

6 were highly regarded experts in the field, clinical situations might not be similar to the Dutch situation and their expert opinion might not be shared. This could limit the generalizability and practicality of the list, but emphasises that continued discussions and research on treatment-limiting decisions are essential.

Textbox 1: Reasons, including potential outcome perspectives, to strongly consider treatment-limiting decisions (chapter 6) [47]

1. Brain death, from a patient's perspective (not considering interests regarding organ donation procedures). [99,100]
2. (chronic) Unresponsive wakefulness syndrome. [96,101]
3. Minimally conscious state – (minus) (i.e. visual pursuit, localization of noxious stimuli, appropriate smiling or crying to emotional stimuli). [101,102]
4. An available, unquestionable, written and signed specific advance directive of the patient that prohibits treatment in a specific situation (possibly related to expected outcome).
5. A proxy opinion that is unquestionably based on patient preferences and that is not in conflict with the attending medical teams' considerations, that prohibits treatment in a specific situation (possibly related to expected outcome).
6. A patient's view (or when necessary a reconstructed vision through surrogated) on life and quality of life is contrary to the outcome that can be expected from the best available prognostic models.
7. From a societal perspective, treatment costs along the whole chain of care that are not cost-effective and higher than the maximum amount that has been decided by national legislation.

The societal perspective

Second, treatment can be considered disproportional from a societal perspective. Healthcare is not only about individuals but also about improving health of populations. [12-14,32] The proposed strategy of providing acute treatment to more s-TBI patients is likely to substantially increase in-hospital costs. On a large scale, this might affect restricted healthcare budgets and jeopardize vulnerable healthcare systems or societal health. [3,103] This is undesirable in a time where politicians are already struggling to restrict the increasing worldwide economic burden of healthcare. [103] Despite governmental restrictions, The Netherlands, with 17.3 million inhabitants

in 2019, spent as much as €80.9 billion on healthcare in 2019, an increase of 4.8% compared to 2018. [104] This accounts for 10% of total gross domestic product [104], similar to many other high-income countries: 11.5% (9.6% – 12.4). [103] Although treating more s-TBI patients could be legitimized by more patients with improved and hopefully 'acceptable' outcome, the future of healthcare systems requires prudence and optimal use of restricted resources.

Justice, as one of four moral principles in medical ethics (Table 3), requires the fair distribution of benefits, risks and limited medical goods and services. [105-107] With respect to its many variations, this is in line with the principle of utilitarianism, which seeks to maximize the well-being of most of the people, instead of the individual. [108,109] Incorporating these principles in acute treatment decision-making could mean that resources, potentially beneficent for an individual patient, are ethically restricted for the wellbeing of the entire society. In line with this, resources should not be used on so-called ineffective and disproportional treatments in s-TBI patients with a very low chance of achieving 'acceptable' outcome, because it will deprive other patients of potentially effective treatments. [110] Cost-effectiveness analyses and concepts such as value-based healthcare can be used to substantiate acute treatment decision-making and prevent inefficient use of limited healthcare resources.

Table 3: Moral principles in medical ethics

Principle	Description
1. Autonomy	A norm of respecting and supporting autonomous decisions.
2. Beneficence	A group of norms pertaining to relieving, lessening, or preventing harm and providing benefits and balancing benefits against risks and costs.
3. Nonmaleficence	A norm of avoiding the causation of harm.
4. Justice	A group of norms for fairly distributing benefits, risks, and costs.

In-hospital costs

The true cost-effectiveness and feasibility of the proposed strategy has not been investigated in *this thesis*, and also remains unknown based on the in-hospital healthcare consumption and in-hospital costs that are reported in *chapter 3, 4 and 5*. [6,7,111] It is also difficult to make statements based on available literature, since cost-effectiveness literature in s-TBI is scarce and inconclusive. Some studies report TBI treatment to be cost-effective [112-115], while others report the opposite. [113,116] The feasibility of the proposed strategy remains unclear and requires further investigation with actual cost-effectiveness analyses.

Cost-effectiveness aside, the average in-hospital costs of s-TBI patients (€26,595) [6] that would be associated with the proposed strategy seem to be acceptable compared to the in-hospital costs for other diseases in the Netherlands. Costs were lower compared to the in-hospital costs of s-TBI for patients with ischaemic stroke (€5.328) [117], transient ischaemic attack (€2.470) [117], appendicitis (€3.700), colorectal cancer (€9.777 – €19.417) [118], percutaneous coronary intervention (€14.037) or coronary artery bypass grafting (€17.506) [119]. In-hospital costs were higher for patients with non-small cell lung cancer (€33.143) [120], ipilimumab treatment in melanoma patients (€73.739) [121] or patients receiving extracorporeal life support treatment (€106.263). [122]

Costs also seem to be acceptable when comparing the in-hospital costs for s-TBI patients with the Dutch cut-off point for cost-effective treatments of €80.000 per Quality-adjusted Life Year (QALY). [123] Although the comparison of reported in-hospital costs with the €80.000 cut-off point for cost-effectiveness analyses is not entirely appropriate, and although there are always few patient outliers with very high costs, the costs of nearly every TBI patient studied in *this thesis* was lower than €80.000.

Both comparisons are illustrative, but have obvious limitations. First, analyses should not only assess in-hospital costs, but all costs associated with s-TBI, including out of hospital and other indirect costs. Only using in-hospital costs results in a major underestimation of the total costs related to s-TBI. Especially when patients survive with severe disabilities, chronic care after hospital discharge, but also loss of productivity, have substantial economic and societal impact.

Including an economic perspective in decision-making is regarded as reasonable because of its objectivity. Focusing on the economic perspective however also fails to recognize individual aspects of care and the social utility of caring for those most in need. People obtain benefit from the belief that they live in a compassionate and humane society where patients in need will not be ignored merely based on costs. Still, there must be a point where TBI is so severe and patient outcome so 'unacceptable' that it does not justify the associated costs. For future decision-making, it would be very helpful to know where that point is.

FUTURE RESEARCH

The treatment of patients with s-TBI deserves scientific and public attention given the considerable medical and economic burden for patients, proxies, and societies. Treatment decision-making will benefit most from knowing which specific patient will benefit from which specific treatment in terms of cost-effectiveness and patient outcome. Accurate prognostication and the determination of the 'acceptability' of outcome are essential parts of the acute treatment decision-making process. Future studies should focus on investigating:

1. New diagnostic and treatment modalities including their (cost-) effectiveness and their effect on short- and long-term patient outcome. [124,125]
2. The (patho)physiological mechanisms of brain injury and it's plasticity. [3,126-130]
3. Reliable, reproducible, validated, free and easy to use outcome assessment tools that are sensitive for disabilities commonly present in s-TBI survivors. [52]
4. Methods to improve the reliability of prognostic or machine learning models. [131,132]
5. The influence of human values, including a dignified existence and the wellbeing of patients, proxies and society.

Different study designs will be required to answer different research questions. Randomized controlled trials (RCTs), the cornerstone of evidence-based medicine, might provide answers to point 1, 3 and 4. Although very little translatable evidence has been derived from 191 completed RCTs for acute TBI management [133], more sophisticated large multi-centre RCTs in priority areas might still be able to make a valuable contribution. [133]

To allow RCTs in the hyper acute setting of TBI and to increase their quality, efficiency and contribution to the evidence base, optimized research protocols are needed to overcome several complicating factors in the acute and stressful setting, such as; unavailable necessary information (i.e. trauma mechanism, medical history, use of anticoagulants), and a patients' inability to provide informed consent. A rigorous research protocol is essential for any study to be successful and to obtain institutional review board approval. The increased use of informed consent alternatives, such as deferred consent or exception from consent, has the potential to improve efficiency and quality of future emergency interventional studies in patients with an inability to provide informed consent. [134]

Another method to answer research questions related to point 1 and 4 is called "Comparative Effectiveness Research" (CER). With this method, the effectiveness of (surgical and critical care) treatment is investigated by comparing variation between local practices. This method is used in recent TBI research initiatives like CENTER-TBI, TRACK-TBI and Net-QuRe. [119,135,136] CER is a well-known and promising method to assess treatment effectiveness in TBI, but there are also some important limitations. [137] Studies are generally expensive because many centres and participants must be included to reach sufficient statistical power. Also, effect estimates largely depend on the used analytical method. When a RCT or CER design is not possible, the focus should be on patient cohorts, surgical treatments and outcome measures that are as equal as possible. It is highly recommended to use the well-known common data elements. [138] This will improve comparability and generalizability of study results and allow data analyses in large meta-analyses. Point 2 is basically fundamental research and point 3 and 5 require a more humanistic approach to the topic.

CONCLUSION

Decision-making dilemmas in the acute treatment of s-TBI patients are common. They are caused by insufficient evidence and by uncertainties in outcome prediction and outcome valuation. To decrease uncertainty and improve decision-making, treatment-limiting decisions in a selection of s-TBI patients should be delayed to after at least 72 hours after injury. These patients will receive optimal acute treatment. Although the feasibility and cost-effectiveness of the proposed strategy requires further investigation, it prevents premature treatment-limiting decisions and allows the collection of essential information to improve the identification of patients that will benefit from specific treatment strategies. At the same time, it could prevent 'unacceptable' patient outcome and inefficient use of limited healthcare resources in threatened healthcare systems. Including an economic perspective in decision-making is reasonable and essential, but the individual aspects of care and the social utility of caring for those most in need should not be disregarded. Although it is unlikely that all uncertainty will ever be resolved, researchers and ethicists should continue to try to reduce uncertainty in decision-making by improving the scientific quality of evidence.

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